UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,823	07/08/2005	Andreas Katopodis	TX/4-32561A	4724

1095 7590 11/24/2008

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
BELYAVSKYI, MICHAIL A	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
11/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,823	KATOPODIS ET AL.	
	Examiner	Art Unit	
	Michail A. Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *1 and 3-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 08/28/08 is acknowledged.

Claims 1-13 are pending.

2. Claims 1, 3-12 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 2 and 13 read on a method for inducing hematopoietic chimerism in a recipient of cells comprising administering to the recipient bone marrow cells, a LFA-1 inhibitor in combination with costimulation inhibitor or mTOR inhibitor are under consideration in the instant application.

In view of the amendment, filed 08/28/08 the following rejections remain

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:
A person shall be entitled to a patent unless --

(e)) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 37(c) of this title before the invention thereof by the applicant for patent.

4. Claims 2 and 13 are rejected under 35 U.S.C. 102(e) as being anticipated by WO' 01/95928(IDS) for the same reasons set forth in the previous Office Action, mailed on 02/26/08.

Applicant's arguments, filed 08/28/08 have been fully considered, but have not been found convincing.

Applicant asserts that the methods of WO'928 only involves the steps of administering a first agent, i.e. CE28,CTLA4 or B7 molecules; the second agent is a molecule that recognized and binds CD40 or CD154 and the third agent is a molecule that interferes with LFA-1 adhesion molecule.

Contrary to Applicant's assertion, it is noted that WO'928 provides a methods for regulating immune system diseases such as those associated with allograft transplantation (see page 4 in particular). At page 12, WO' 928 teaches that immune system diseases refer to various diseases such as the result from bone marrow transplantation or tissue or cell allo-or xenograft including solid organ, skin etc. In other words, the method of WO'928 inherently comprises of administering of bone marrow cells in addition to the other three agents that are acknowledged by Applicant, i.e. anti-LFA antibody, anti CD154 antibody and immunosuppressant.

The reference teaching anticipates the claimed invention.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negstived by the manner in which the invention was made.

6. Claims 2 and 13 stand rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,653,282 or WO 95/34320 each in view of US Patent 6,486,209 and US 2002/01524900 for the same reasons set forth in the previous Office Action, mailed on 02/26/08.

Applicant's arguments, filed 08/28/08 have been fully considered, but have not been found convincing.

Applicant asserts that : (i) US'282 does not teach or suggest the additional administration of bone marrow cells or other precursor cell to a recipient of cells, tissue or organ transplant; (ii) WO' 320 does not teach or suggest the use of anti-CD154 antibody. (iii) US '490 only teaches a tissue construct for implantation. There is no teaching or motivation to choose administering 15-deoxyspergualine in combination with CD154 antibody.

Applicants have traversed the primary and the secondary references pointing to the differences between the claims and the disclosure in each reference. Applicant is respectfully reminded that the rejection is under 35 USC103 and that unobviousness cannot be established by attacking the

references individually when the rejection is based on the combination of the references. see In re Keller, 642 F.2d 4B, 208 USPQ 871, 882 (CCPA 1981) See MPEP 2145. This applicant has not done, but rather argues the references individually and not their combination. One cannot show non-obviousness by attacking references individually where the rejections are based on a combination of references. In re Young 403 F.2d 759, 150 USPQ 725 (CCPA 1968).
Applicant is reminded that as stated in MPEP § 2123, "The use of patents as references is not limited to what the patentees describe as their own inventions or to the problems with which they are concerned. They are part of the literature of the art, relevant for all they contain." In re Heck, 699 F.2d 1331, 1332-33, 216 USPQ 1038, 1039 (Fed. Cir. 1983) (quoting In re Lemelson, 397 F.2d 1006, 1009, 158 USPQ 275, 277 (CCPA 1968)).

Moreover, it has been recently stated that KSR forecloses the argument that a specific teaching, suggestion, or motivation are required to support a finding of obviousness See Board decision (see *KSR International Co v Teleflex Inc*., 550U.S.-, 82 USPQ2d 1385, 2007).

US Patent '282 teaches a method of inducing immune tolerance during organ, tissue or cell transplantation including bone marrow transplantation, i.e. inducing hematopoietic chimerism, comprising administering to the subject a combine therapy of LFA-1 inhibitor and co-stimulatory inhibitor (see entire document, Abstract, and column 2 in particular).

WO' 320 teaches a method of inducing immune tolerance during organ, tissue or cell transplantation, including bone marrow transplantation, i.e. inducing hematopoietic chimerism, comprising administering to the subject a combine therapy of LFA-1 inhibitor and co-stimulatory inhibitor(see entire document, Abstract and pages 3, 4, 8, 19 and 22 in particular).

With regards to Applicant's comments that WO' 320 does not teach or suggest the use of anti-CD154 antibody.

WO'320 teaches that the use of combination therapy of LFA-1 antibody and second agent that is costimulation inhibitory agent (see page 19 in particular). At the time the invention was made one skill in the art would know that one of costimulation inhibitory agent is anti-CD154 antibody that specifically recognized and binds to CD40

The claimed invention differs from the reference teaching in that US Patent '282 or WO' 320 does not exemplify teaches a method of inducing hematopoietic chimerism, comprising administering a combination of LFA-1 inhibitor, co-stimulation inhibitor and immunosuppressive inhibitor 15-deoxyspergualine.

US Patent ' 209 teaches a method of transplantation of organ, tissue or cell comprising administering to the subject an immunosuppressive inhibitor 15-deoxyspergualine (see entire document, Abstract, column 5 and claim 1 in particular).

US '490 teaches a method for inducing hematopoietic chimerism in a subject comprising administering a conventional immunosuppressant treatment using 15-deoxyspergualine (see entire document, page 4 in particular).

All the claimed elements were known in the prior art and one skill in the art could have combine the elements as claimed by known methods with no change in their respective function and the combination would have yield predictable results to one of ordinary skill in the art at the time of the invention (see *KSR International Co v Teleflex Inc*., 550U.S.-, 82 USPQ2d 1385, 2007).

Thus it would have been obvious to one of the ordinary skill in the art at the time the invention was made to combine a conventional immunosuppressant treatment with 15-deoxyspergualine and a combination of LFA-1 inhibitor and co-stimulation inhibitor (anti-CD28 or anti-CD40/CD154, etc) for inducing hematopoietic chimerism with a reasonable expectation of success. "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. . . [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205USPQ 1069, 1072 (CCPA 1980) (see MPEP 2144.06).

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

The following new ground of rejection are necessitated by the amendment filed 08/28/08.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 2 and 13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a New Matter rejection**.

" **additionally** administering to the recipient: i) bone marrow cells or other precursor cells from the donor and ii) an anti-LFA-1 antibody in combination with...." claimed in 2 represent a departure from the specification and the claims as originally filed and applicant has not pointed out where the support come from.

The Specification and claims only support " A method for inducing hematopoietic chimerism in a recipient of cell, tissue or organ transplant comprising administering : i) bone marrow cells or other precursor cells from the donor and ii) an anti-LFA-1 antibody in combination with... "

9. No claim is allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on 571/ 272-0878.

The fax number for the organization where this application or proceeding is assigned is 571/273-8300

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Michail A Belyavskyi/
Primary Examiner, Art Unit 1644